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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/402,820	10/12/99	CHAIN	D CHAIN=1B

001444 HM12/0523
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EXAMINER	
DUFFY,P	
ART UNIT	**PAPER NUMBER**
1645	10

DATE MAILED: 05/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/402,830	Chain
Examiner	**Group Art Unit**
DUFFY	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3-14-01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-31 is/are pending in the application.

Of the above claim(s) 1-13, 15-22 and 26-31 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 14, 23-25 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-31 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachm nt(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3x

☐ Interview Summary, PTO-413

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Oth r _____

Office Acti n Summary

DETAILED ACTION

1. The Group and/or Art Unit of U.S. Patent application SN 09/402,820 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Art Unit 1645.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

3. The drawings submitted with this application have be approved by the draftsperson.

Election/Restriction

4. Applicant's election of Group II in Paper No. 10, mailed 3-14-01 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-13, 15-22 and 26-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112

5. Claims 14 and 23-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite "end-specific for the terminus of an amyloid β peptide (Aβ)" monoclonal or single chain antibodies. However, it is well established in this art area that Aβ peptide refers to a heterogenous population of amyloid peptides wherein both the N- and C-terminals are heterogenous. For example, the art of record refers to both Aβ (1-40) and Aβ (1-42) that documents the heterogeneity at the C-terminus. Similarly, the art of record documents the heterogeneity at the N-terminus. Thus, in the absence of a defined specific sequence epitope to which the antibody binds the metes and bound of "end-specific for the N-terminus or C-terminus of an amyloid β peptide" can not be ascertained.

Claim Rejections - 35 USC § 102 or 103

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 14 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995; reference AC on PTOL-1449 filed 12 October 1999) or Koing et al (Ann NY Acad. Sci., 777:345-355, 1996; reference AH on PTOL-1449 filed September 25, 2000) or Tsuzuki et al (Neuroscience Letters, 202:77-80, 1995; reference AQ on PTOL-1449 filed September 25, 2000).

Takeda et al teach monoclonal antibodies that are specific for the N-terminal and C-terminal of Aβ (see page 5, first full paragraph, lines 9-20). Antibodies designated BAN-052a and BAN-50a bind the C-terminal but not the N-terminal of Aβ . Antibodies designated BA-27a, BS-85a and BC05a bind the N-terminal but not the C-terminal of Aβ (see Tables 1-4 and pages 30-35, in regard to specificity studies). Takeda teaches the combination of end-specific antibodies to detect Aβ (1-40) and Aβ (1-42) for the detection of Aβ species *in vitro*.

Koing et al teach monoclonal antibodies that are specific for the N-terminal (MAb 286.8A) and C-terminal (MAb 369.2B) of Aβ (see page 347, Table 1 for binding specificities). Koing et al teach the use of end-specific antibodies for the detection of Aβ peptides *in vitro*.

Tsuzuki et al teach a monoclonal antibody that binds Aβ (1-9) (see abstract and page 78, column 1, second full paragraph). Tsuzuki et al teach the use of end-specific antibodies for the detection of Aβ peptides *in vitro*.

9. Claims 14, 23 and 25 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Solomon et al (U.S. Patent 5,688,651, issued 11-18-1997, filed December 16, 1994).

Solomon et al teach a monoclonal antibody AMY-33 that is specific for the N-terminal (amino acids 1-28) of Aβ (see column 6, third full paragraph) . Solomon et al teach and contemplate the a single chain antibody based on the AMY-33 monoclonal antibody (see column

7, lines 9-11) and their use as therapeutic chaperones for the treatment of Alzheimer's Disease (see column 16, fourth and fifth full paragraphs).

10. Claims 14 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999), Koing et al (Ann NY Acad. Sci., 777:345-355, 1996) or Tsuzuki et al (Neuroscience Letters, 202:77-80, 1995; reference AQ on PTOL-1449 filed September 25, 2000) in veiw of Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Duenas et al (BioTechniques, 16(3):476-483, 1994).

The claims are drawn to single chain antibodies that are end-specific for Aβ peptides.

Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999), Koing et al (Ann NY Acad. Sci., 777:345-355, 1996) and Tsuzuki et al (Neuroscience Letters, 202:77-80, 1995; reference AQ on PTOL-1449 filed September 25, 2000) are set forth *supra*. Takeda and Koing et al differ by not teaching recombinantly produced single chain antibodies.

Seubert et al teach the use of antibodies that bind Aβ peptides are useful in the diagnosis of probable Alzheimer's disease and are useful for detecting Aβ peptides in *in vitro* or *in vivo* assays that screen for inhibitors of Aβ peptide formation (see columns 4-5, Summary of the Invention). Seubert et al teach that in addition to monoclonal antibodies, "...the detection techniques of the present invention will also be able to use antibody fragments, such as F(ab), Fv, V_L, V_H, and other fragments." Seubert et al also teach that "It will also be possible to employ recombinantly produced antibodies (immunoglobulins) and variations thereof as now well described in the patent and scientific literature. See, for example, EPO 8430268.0; EPO

85102665.8; EPO 85305604.2; PCT/GB 85/00392; EPO 85115311.4; PCT/US 86/002269; and Japanese application 85239543." (see column 10, first full paragraph).

Duenas et al teach art accepted conventional methods of intra- and extracellular expression of an single chain Fv antibody fragment (scFv) in *E. coli*. Duenas et al teach that cloning of immunoglobulin variable regions and bacterial expression of antibody fragments was routinely performed in the art at the time that this invention was made (see page 476, column 2, Introduction).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that this invention was made to modify the end-specific monoclonal antibodies of any one of Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999), Koing et al (Ann NY Acad. Sci., 777:345-355, 1996) or Tsuzuki et al (Neuroscience Letters, 202:77-80, 1995; reference AQ on PTOL-1449 filed September 25, 2000) as set forth *supra* by means of expression as a single chain Fv antibody fragment (scFv) according to the vectors and methodology of Duenas et al because Seubert et al teach that Fv and other antibody fragments including those that have been recombinantly produced that bind Aβ peptides are useful in a variety of detection techniques for use in screening or diagnostic assays.

Status of Claims

11. No claims are allowed.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice

published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308-3909.

Patricia A. Duffy, Ph.D.
May 17, 2001

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600